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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/755,639

01/12/2004

John P. Wikswo

14506-44211

1080

24728 7590 03/28/2008  
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EXAMINER

BOWERS, NATHAN ANDREW

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

03/28/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/755,639	<b>Applicant(s)</b> WIKSWO ET AL.	
	<b>Examiner</b> NATHAN A. BOWERS	<b>Art Unit</b> 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 10-20 and 23-81 is/are pending in the application.
- 4a) Of the above claim(s) 25-74 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 10-20, 23, 24 and 75-81 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 25 January 2008 has been entered.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1-4, 6, 10-15, 17, 19, 23, 24, 75, 76 and 78-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodgson (US 20030107386) in view of Klemic (US 6699697).

With respect to claims 1, 2, 75 and 76, Dodgson discloses a device for monitoring the status of at least one cell. The apparatus comprises a first substrate, a second substrate supported by the first substrate, and a first passage formed within the body of the second substrate. An opening is formed on the first surface of the second substrate such that the first passage is in fluid communication with a reaction area formed above the second substrate. Paragraphs [0009] and [0010] state that electrodes (Figure 3:24,26) are provided to detect the presence of a cell (Figure 3:16) to be tested. A third substrate is positioned above the second substrate to define a reaction area therebetween, and a second passage is formed below the third substrate in fluid communication with the reaction area. This is apparent from Figure 3. Paragraph [0036] clearly states that at least one seal element (Figure 3:22) is positioned on the second substrate and such that it encircles the opening. Another embodiment in Figure 4 depicts a similar apparatus, however, the third substrate is replaced with a sidewall feature. Dodgson does not expressly describe an embodiment in which a third substrate and sidewalls are both formed above the second substrate to define a reaction chamber and a second passage.

Fig.3.

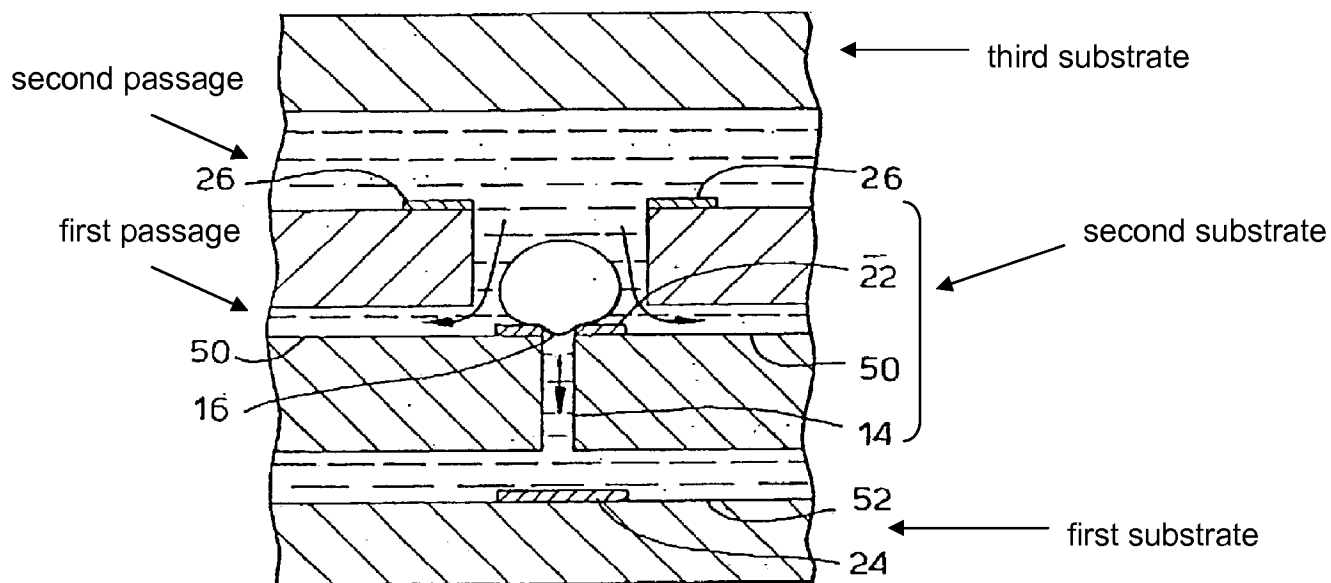
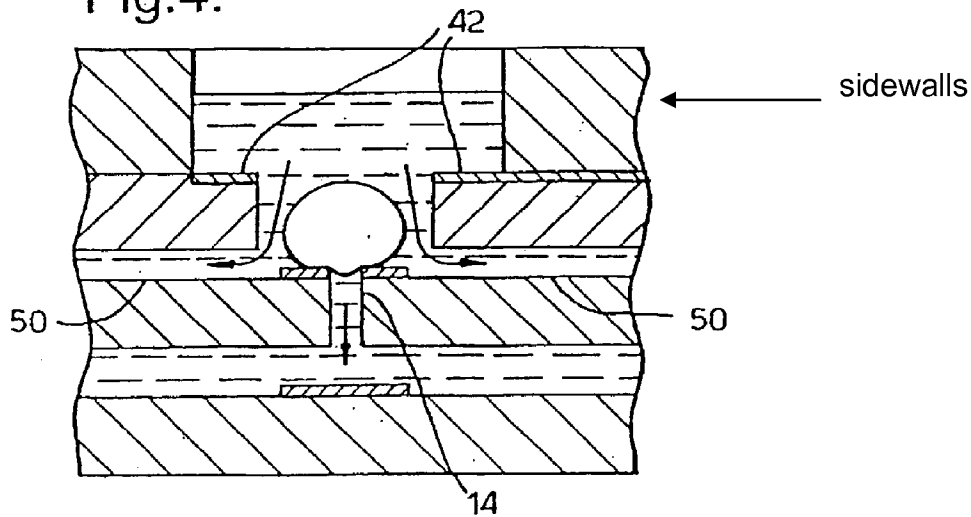


Fig.4.



At the time of the invention, it would have been obvious to alter the construction of Dodgson's device by incorporating features set forth in the embodiments presented in both Figures 3 and 4. It would have been apparent to provide a reaction chamber defined by both a

third substrate and sidewalls, as such construction is considered to be well known and commonly practiced in the art. It would require only minor structural alterations to either of the presented embodiments to form a reaction chamber and second passage bound by both a sidewall area and a third substrate.

The apparatus of Dodgson, however, still differs from Applicant's claimed device because Dodgson does not expressly describe a first pair of fluid controls positioned in the first passage and a second control positioned inside the second passage. Although paragraph [0043] of Dodgson describes the use of valves generally, Dodgson does not clearly disclose their relationship to the first and second passages.

Klemic discloses a device for monitoring the status of at least one cell. Klemic teaches that a first substrate in the form of a backplate is provided. A second substrate in the form of a dual PDMS layer is supported by the backplate. Column 6, lines 19-35 indicate that the second substrate includes a plurality of microfluidic channels, thus forming at least one first passage in the second substrate. The PDMS second substrate is formed from "a single PDMS sheet containing both the cell interface aperture and the microfluidic channels and/or valves." Sidewalls and a third substrate are formed above the second substrate in order to form a chamber. This is apparent from Figures 1-3 and 10. Klemic further states in column 14, lines 26-67 that valves are used to regulate the flow of fluids to and from the examination site.

Dodgson and Klemic are analogous art because they are from the same field of endeavor regarding patch-clamp apparatuses.

At the time of the invention, it would have been obvious to ensure that the first and second passages disclosed by Dodgson are controlled using automated valves. As evidenced by Klemic, the use of fluid flow control systems is well known in the art. In the apparatus of Dodgson, valves would serve to precisely control the amount of fluid moved to the cell monitoring location. Valves would allow one to move desired compounds to the cell so as to determine their effect on cellular activity.

With respect to claims 3, 4 and 6, Dodgson and Klemic disclose the apparatus set forth in claim 2 as set forth in the 35 U.S.C. 103 rejection above. In addition, Dodgson states that the electrode sensing elements further act as an electroporation device capable of stimulating cells positioned within the reaction area. This is taught in paragraph [0039]. A medium is introduced to the reaction area through the second passage such that the sensor measures the response of the cell to the medium. Paragraph [004] states that variations in the medium cause a variation in the impedance of the cell in the reaction area.

With respect to claims 10 and 11, Dodgson and Klemic disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. Although Dodgson does not expressly disclose the use of reservoirs in communication with the first and second passages, it is understood that the use of reservoirs as supply medium containers and waste containers is notoriously well known in the art. In fact, Klemic states in paragraphs [0168]-[0172] that reservoirs are used to hold fluid until the fluid is pumped to the cell monitoring location.

With respect to claims 12-15, 17, 19, 23, 24 and 78-80, Dodgson and Klemic disclose the apparatus as previously described above. Dodgson additionally states in paragraphs [0010], [0013] and [0014] that a plurality of chambers are defined by the first, second and third substrates. An array of chambers is formed such that each chamber includes a sensor/poration electrode capable of detecting impedance and electrically stimulating a cell. Each chamber is connected to neighboring chambers via the second passage formed by the third substrate and the sidewalls. Klemic additionally indicates in columns 19 and 20 that it is known to provide an array of monitoring locations linked in fluid communication with one other.

2) Claims 5, 7, 16, 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodgson (US 20030107386) and Klemic (US 6699697) as applied to claims 2 and 12, and further in view of Rubinsky (US 6482619).

Dodgson and Klemic disclose the apparatus set forth in claims 2 and 12 as set forth in the 35 U.S.C. 103 rejections above, however do not expressly state that fluid moves through the first passage to the cell. Dodgson teaches that fluid moves through the first passage away from the cell (See Figures 3 and 4).

Rubinsky discloses a device for monitoring the status of a least one cell. Rubinsky discloses a substrate (Figure 1:11) comprising a body portion that defines a first passage (Figure 1:13) and an opening (Figure 1:18) in communication with the first passage. Another substrate (Figure 1:17) further defines a chamber and a second passage (Figure 1:16) formed between the substrates. This is disclosed in column 17, lines 11-27. Rubinsky teaches in column 17, lines



28-42 that the first and second passages each carry a fluid medium to a cell at the opening in order to determine the response of the cell to each medium.

Dodgson, Klemic and Rubinsky are analogous art because they are from the same field of endeavor regarding cell monitoring systems.

At the time of the invention, it would have been obvious to alter the apparatus of Dodgson in order to allow the addition of fluids to both the first and second passages. It would have been beneficial to add fluids to the reaction chamber via the first and second passages because this would have allowed one to simultaneously test the effects of multiple compounds on analytes within the chamber.

3) Claims 77 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dodgson (US 20030107386) and Klemic (US 6699697) as applied to claims 1 and 12, and further in view of Wang (US 20020182627).

Dodgson and Klemic disclose the apparatus set forth in claims 1 and 12 as set forth in the 35 U.S.C. 103 rejections above. Dodgson teaches that the body portion of the second substrate further defines an intersection portion where the first passage and the opening on the first surface of the second substrate are in fluid communication. Dodgson, however, does not expressly state that the intersection is partially formed as a cone shaped portion.

Wang discloses a device for monitoring the status of at least one cell. Wang discloses the use of a substrate (Figure 2:10) that includes an opening (Figure 2:12) used to link first and second fluid passages. From Figure 2, it is apparent that this intersection point is at least partially formed as a cone shaped portion (Figures 2B-2E).

Dodgson, Klemic and Wang are analogous art because they are from the same field of endeavor regarding cell monitoring systems.

At the time of the invention, it would have been obvious to alter the apparatus of Dodgson to ensure that a portion of the second substrate was formed in the shape of a cone. Cone shapes serve to funnel cells towards the opening where they then form a seal. Mere changes in shape are generally not sufficient to distinguish over the prior art when the changes in shape do not produce a distinctly different mode of operation. See MPEP 2144.04.

### ***Response to Arguments***

Applicant's arguments filed 25 January 2008 with respect to the 35 U.S.C. 103 rejections involving Dodgson have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the combination of Dodgson with Klemic.

Klemic addresses the deficiencies of Dodgson by clearly indicating that control mechanisms are provided for adding and removing fluids to and from the cell monitoring site of a patch clamp apparatus. Klemic additionally indicates that reservoirs widely used in the art to supply and collect fluids perfused through microfluidic systems. It would have been obvious to provide valves at the first and second passages disclosed by Dodgson in order to deliver various fluids and compounds to the cell at predetermined times. It would also have been obvious to ensure that fluid reservoirs are used to supply desired compounds and collect wastes.

Applicant's remaining arguments with regard to the Dodgson reference have been fully considered but they are not persuasive.

*Applicant's principle arguments are*

*(a) Dodgson does not describe a single embodiment in which sidewalls and a third substrate are positioned over a second substrate in order to form a chamber and a second fluid passage.*

In response to Applicant's arguments, please consider the following comments.

As previously stated above, it would have been obvious to alter any of the embodiments set forth by Dodgson in order to produce a chamber and a second fluid passage using a third substrate positioned over a second substrate. Dodgson indicates in Figure 4 that it is beneficial create a chamber for holding cells using sidewalls. Dodgson additionally indicates in Figure 3 that it is likewise beneficial to create a fluid passage between the second and third substrates that is capable of transporting various chemical agents to the cell. Accordingly, it would have been obvious to combine these two structures in order to avail oneself of the advantages of each.

*(b) No fluid communication exists between the intracellular space of the object 30 and channel 14, which teaches away from the instant invention.*

In response to Applicant's arguments, please consider the following comments.

In the apparatus of Dodgson, an object/cell is positioned at an orifice formed at the first passage. Accordingly, the exterior of the cell is undoubtedly in fluid communication with the first passage. Since cell membranes are naturally characterized by various pores and channels, it must be concluded that the interior of the cell is likewise in fluid communication with the first

passage. Electroporation procedures enhance the porosity of the cell membrane, and thereby would serve to increase this natural fluid communication.

Applicant's arguments with regard to the combination of Dodgson and Rubinsky have been fully considered but they are not persuasive.

*Applicant's principle arguments are*

*(a) Dodgson does not teach or suggest that fluid moves through the first passage to the cell, but instead teaches away from this type of device.*

In response to Applicant's arguments, please consider the following comments.

It is agreed that Dodgson states that the first passage is used to remove fluid from the chamber. Dodgson states that a medium is introduced to the chamber via the second passage, and that the first passage is used to withdraw the fluid in order to create a suction that traps the cell at the orifice. However, the Rubinsky reference teaches that this arrangement is not necessary to successfully trap a cell at an orifice during examination. Figure 1 of Rubinsky clearly suggests that fluid is moved to a cell located at an orifice using both a first and second passage. Like Dodgson, Rubinsky also teaches that a tight seal between the cell and orifice is required, however Rubinsky does not require the withdrawal of fluids through the lower first passage in order to create this seal. Rubinsky is evidence that fluid could be added to the system of Dodgson using both the first and second passages without destroying the functionality of the Dodgson apparatus.

Applicant's arguments with regard to the combination of Dodgson and Wang have been fully considered but they are not persuasive.

*Applicant's principle arguments are*

*(a) Applicant respectfully submits that Wang is not a qualified reference because it is unclear if Wang benefits from the priority date established by U.S. provisional application number 60/278,308.*

In response to Applicant's arguments, please consider the following comments.

Figure 2 in U.S. provisional application number 60/278,308 is identical to that set forth in Wang 2002/018627. From this, it is clear that Wang anticipated the use of a cone shaped substrate member in provisional application number 60/278,308.

### ***Conclusion***

This is a non-final rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nathan A Bowers/  
Examiner, Art Unit 1797

/Jill Warden/  
Supervisory Patent Examiner, Art Unit 1797